

Remarks

A. Status of the Claims

Claims 29-43 are currently pending. Claim 29 has been amended to more precisely define the method by which the optical signal produced by the reporter molecule is quenched. In particular, claim 29 has been amended to clarify that the optical signal produced by the reporter molecule is quenched by the aptamer's conformation and not by means of a separate quenching molecule covalently coupled to the signaling aptamer.

As described in the present specification, the aptamers of the present invention do not incorporate a separate molecule to mediate the optical signal produced by the reporter molecule (*see e.g.*, p 17, ln. 1 to p. 18, ln. 10; p. 20, ln. 13 to p. 22, ln. 8; and FIGs. 2A and 2B). The working examples provided in the present specification demonstrate that a ligand-dependent differential optical signal can be produced by a signaling aptamer in which a single reporter molecule has been covalently appended. For example, the signaling aptamer ATP-R-Ac13 has a single acridine moiety introduced in the place of the adenosine at position 13 of the aptamer (*see* p. 21, ln. 16-18, and FIG. 2A). The signaling aptamer DFL7-8 has a single fluorescein molecule inserted between residues 7 and 8 of the aptamer (*see* p. 21, ln. 18 to p. 22, ln. 2, and FIG. 2B). As can be seen from the description of the preparation of these aptamers, quencher molecules were not incorporated into their sequences (*see e.g.*, p 17, ln. 1 to p. 18, ln. 10; p. 20, ln. 13 to p. 22, ln. 8; and FIGs. 2A and 2B). The ATP-R-Ac13 and DFL7-8 aptamers showed marked increases in fluorescence intensity in the presence of their ligand (p. 22, ln. 6-8). Thus, the aptamers of the presently claimed invention do not require a separate quencher molecule appended to the aptamer to mediate the optical signal produced by the reporter molecule.

Applicant further notes that negative limitations are appropriate so long as the boundaries of patent protection sought are clear and negative limitation has a basis in the original disclosure. MPEP § 2173.05(i). The Federal Circuit has noted that “[if] a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met.” *In re Alton*, 76 F.3d 1168, 1175, 37

USPQ2d 1578, 1584 (Fed. Cir. 1996). In view of the passages from the disclosure cited above, it would have been clear to a person of ordinary skill in the art that the present inventor was in possession of a method in which the optical signal produced by the reporter molecule is quenched by the aptamer's conformation and not by means of a separate quenching molecule covalently coupled to the signaling aptamer.

B. Rejections Under 35 U.S.C. §102(e)

Claims 29-37 and 40-43 were rejected under § 102(e) as being anticipated by Gold et al (U.S. Patent No. 6,242,246). Applicant respectfully traverses this rejection.

Gold does not teach a method that comprises providing a signaling aptamer comprising a reporter molecule covalently coupled to an aptamer, wherein in an unbound state an optical signal produced by the reporter molecule *is quenched by the aptamer's conformation and not by means of a separate quenching molecule covalently coupled to the signaling aptamer*, relative to the optical signal produced by the reporter molecule when the aptamer undergoes a conformational change upon binding to its ligand. Rather, Gold discloses a method for quenching a fluorescent molecule using "an energy transfer pair" (Column 13, lines 41-42; FIG. 5). For example, FIG. 5 of Gold, which the Action cited in support of its §102(e) rejection on page 4, discloses a quenching molecule (52) in close proximity to the fluorescence molecule (53). In contrast, FIGs. 2A and 2B of the present specification disclose a fluorescence molecule (F) *with no quenching molecule*, the absence of which represents an advance over the cited art. An advantage of Applicant's method is that it obviates the need for a quenching molecule to be engineered onto the aptamer.

Because Gold teaches a method whereby the fluorescence molecule is quenched by a quenching molecule rather than by the conformational change itself, Gold does not teach every element of Claim 29. Gold therefore does not anticipate independent Claim 29 or dependent Claims 30-37 and 40-43 under §102(e). Applicant, therefore, respectfully requests the withdrawal of this rejection.

C. Rejections Under 35 U.S.C. §103(a)

Claims 38-39 were rejected under §103(a) as being obvious over Gold as defined by

Pitner (U.S. Patent No. 5,650,275) in view of Szostak (U.S. Patent No. 5,631,146). The Action states that Gold does not teach anti-adenosine aptamers as in claims 38-39. The Action asserts, however, that Szostak teaches anti-adenosine aptamers, and that it would have been obvious to apply the anti-adenosine aptamers of Szostak to the target detection method of Stanton. Applicant respectfully traverses this rejection.

As set forth in the preceding section, the Action does not establish that Gold teaches all of the elements of the method recited in independent claim 29. Thus, regardless of whether it would have been obvious to apply the anti-adenosine aptamers of Szostak to the target detection method of Gold, the Action still fails to establish that these references teach or suggest all of the elements of claims 38-39. Applicant, therefore, respectfully requests the withdrawal of this rejection.

D. Conclusion

In view of the above, Applicant submits that all of the claims are in condition for allowance. The Examiner is invited to contact the undersigned attorney at (512) 536-5654 with any questions, comments, or suggestions relating to the referenced patent application.

Respectfully submitted,



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